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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/619,799	07/14/2003	Glenn H. McGall	2719.2012-004	7882

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EXAMINER
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SHIBUYA, MARK LANCE

ART UNIT	PAPER NUMBER
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1639

DATE MAILED: 11/30/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	Application No. 10/619,799	Applicant(s) MCGALL ET AL.	
	Examiner Mark L. Shibuya	Art Unit 1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 7/22/05.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 10 and 23-34 is/are pending in the application.
- 4a) Of the above claim(s) 10 and 30 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 23-29 and 31-34 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date <u>10/17/2003</u> . | 6) <input type="checkbox"/> Other: _____  |

### DETAILED ACTION

1. Claims 10, 23-34 are pending. Claims 10 and 30 are withdrawn. Claims 23-29 and 31-34 are examined.

#### *Election/Restrictions*

2. Applicant's election of species (arrays of diverse polymers, polymers that are polynucleotides, substrate that is silicon, solid supports connected to linking groups by spacer groups, spacer groups that are hydroxyalkyltrialkoxysilanes, and an ultimate species of linker with the following structure:



(Reply at p.2), in the reply entered on 7/22/2005, is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Applicant states that Claims 23-29 and 31-34 read on the elected species.

3. Claims 10 and 30 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 7/22/2005.

***Priority***

4. This application is a divisional of 09/102,986, filed 6/22/1998, now abandoned.

***Information Disclosure Statement***

5. The information disclosure statement filed 10/17/2003 fails to comply with 37 CFR 1.98(a)(3) because it does not include a concise explanation of the relevance, as it is presently understood by the individual designated in 37 CFR 1.56(c) most knowledgeable about the content of the information, of each patent listed that is not in the English language. It has been placed in the application file, but the information referred to therein regarding reference number AP, WO 93/04145, has not been considered.

6. The citations of references AZ2 and AR3 as cited in the Information Disclosure Statement (IDS), entered 10/17/2003, are not provided dates of publication and so are lined-out on the IDS; however references AZ2 and AR3 are considered.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 28, 29, 32 and 33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "DMT", which is recited in claim 28, is an abbreviation that should be spelled out.

Claim 32 recites the limitation "the selected regions" in line 1. There is insufficient antecedent basis for this limitation in the claim.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

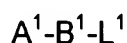
This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 23-29 and 31-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over any of **Kumar et al.**, Tetrahedron Letters, 32 (7): 967-970, 1991 (IDS entered 10/17/2003, reference no. AS3), **Salo et al.**, Collect. Czech. Chem. Commun.,

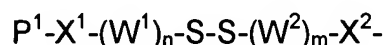
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1996, 61 (Spec. Issue), S110-S111, referred to as **Salo 1**, IDS entered 10/17/2003, reference no. AT3) or **Salo et al.**, Bioconjugate Chem. 1998, Vol. 9, No. 3, pp. 365-371, (referred to as **Salo 2**, IDS entered 10/17/2003, reference no. AU3), each taken separately, and **Lockhart et al.**, US 5,556,752.

The claims are drawn to methods of synthesizing an array of diverse polymers on a substrate, comprising: (a) providing a modified substrate for use in solid phase chemical synthesis, said substrate having the formula:



wherein A is a solid support, B is a bond or a spacer group, and L is a linking group having the formula:



wherein,  $P^1$  is a protecting group;  $X^1$  and  $X^2$  are each independently selected from the group consisting of a bond, -O-, -NH-, -NR- and -CO<sub>2</sub>-, wherein R is a lower alkyl group having one to four carbon atoms;  $W^1$  and  $W^2$  are each independently selected from the group consisting of methylene, oxyethylene and oxypropylene; and n and m are each independently integers of from 2 to 12 with the proviso that n and m are not the same when  $W^1$  and  $W^2$  are the same; and (b) preparing an array of diverse polymers on said modified substrate; and variations thereof.

**Kumar et al.**, Tetrahedron Letters, 32 (7): 967-970, 1991 (IDS entered 10/17/2003, reference no. AS3), throughout the publication, disclose a "solid phase method for the synthesis of oligonucleotide-3'-phosphates (see especially Title, Abstract). Kumar et al. synthesize a "universal Controlled-Pore Glass (CPG)-based

support compatible with established phosphoramidite approach of DNA synthesis", (see page 967). This solid support is unsymmetrical and particularly reads on those claimed (see Scheme 1, compound 6). Note that although the linkage between the solid support and the first sulfur of the disulfide is not species shown in the Scheme, when one looks to the text for the synthesis of this solid support (synthesis of compound 1 from Scheme 1) it is shown that the linkage between the first sulfur of the disulfide and the CPG is accomplished with 3-mercaptopropyltrimethoxysilane (see p. 967, last paragraph and footnote 8 of the reference). Thus the linker of Kumar et al., reads on the instant claims where  $B^1$ =a bond,  $X^1=X^2=O$  and  $W^1=W^2$ =methylene, with  $n=2$  (see compound 6 in Scheme 1) and  $m=3$  (from the mercaptopropyl group). Kumar et al., at p. 968, teach cleavage of the disulfide linkage to the support. Moreover, Kumar et al. disclose that "the disulfide linkage containing polymer support 6 was stable to the coupling, deprotection, capping and oxidative conditions used in the solid phase phosphoramidite chemistry:, (p. 968)). The protecting group ( $P^1$ ) DMT is also disclosed in Kumar et al (see Scheme 1).

**Salo 1**, throughout the publication, discloses asymmetrical disulfide tethered solid supports for oligonucleotide synthesis. See particularly Scheme 1 of Salo 1. The linkers allow for the synthesis of oligonucleotide-3'-phosphates (see, for example, first paragraph) and were tested for their stability. The reference discloses that a chain longer than 2 carbons is needed between the spacer groups and the first sulfur of the disulfide to avoid instability (see p. S111, last paragraph). The reference discloses solid supports where  $P^1$ =DMT,  $B^1$ =a spacer,  $X^1=O$ ,  $X^2$ =a bond and  $W^1=W^2$ =methylene, with  $n$

and m being unequal. Specifically, see compounds 4-11 in Scheme 1 of the reference. Salo 1, at p. S111, teaches the release of oligonucleotides from TentaGel by cleavage of the disulfide linker.

**Salo 2**, throughout the publication, teaches asymmetrical disulfide tethered solid supports for oligonucleotide synthesis. The reference discloses a general scheme for labeling oligonucleotides on a solid support (see Scheme 1) and discloses specific linkers to carry out this process. See particularly Scheme 2 and Table 1 of Salo 2. The linkers allow for the synthesis of oligonucleotide-3'-phosphates (see, for example, Abstract) and were tested for their stability. The reference discloses that a chain longer than 2 carbons is needed between the spacer group and the first sulfur of the disulfide to avoid instability (see Abstract). The reference discloses solid supports where  $P^1$ =DMT,  $B^1$ =a spacer,  $(C(O)NH)$ ,  $X^1=O$ ,  $X^2$ =a bond and  $W^1=W^2$ =methylene, with n and m being unequal. Specifically, see supports S2a-S5b in Table 1 of the reference. Salo 2 at p. 365, notes the use of disulfide based tethers in automated oligonucleotide synthesis and teaches that such tethers withstand basic conditions rather well, and that they readily undergo reductive cleavage.

None of Kumar et al., Salo1 or Salo 2, each taken separately, disclose an array of diverse polymers on a substrate, as in claims 23 and 32, or photolabile protecting groups, as in claims 24-26 and 33.

**Lockhart et al.**, US 5,556,752, throughout the patent, and at col. 14, line 47-col. 15, line 18, teach arrays of oligonucleotides, including those prepared by pin based synthesis, wherein a substrate may be provided with a spacer having active sites, and

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wherein the active sites may be protection optionally with protecting groups, such as Fmoc, BOC, and wherein the spacer may provide for a cleavable function by way of, for example, exposure to acid or base, reading on releasing polymers from the substrate, as in claim 34. Lockhart et al., at, for example, col. 11, 51-67, teach synthesizing libraries on a solid support having a plurality of preselected regions. Lockhart et al., at col. 12, line 1 to col. 13, line 24, teach the use of spacers modified with photolabile groups for light-directed synthesis of polymer arrays on solid supports using, e.g., the VLSIPS method, wherein deoxynucleoside monomers are coupled to produce libraries, as in claim 32 and 33.

It would have been prima facie obvious at the time the invention was made for one of ordinary skill in the art to have used methods comprising a modified substrate having a linker of the formula  $P^1-X^1-(W^1)_n-S-S-(W^2)_m-X^2-$ , as taught by any one of Kumar et al., Salo 1 or Salo 2, each taken individually, and wherein an array of diverse polymers are synthesized onto the linkers, and wherein  $P^1$  is a photolabile protecting group on the linker that is used in coupling monomers of polymers, as taught by Lockhart et al.

One of ordinary skill in the art would have been motivated to use methods for synthesizing arrays on a modified substrate comprising a linker the formula  $P^1-X^1-(W^1)_n-S-S-(W^2)_m-X^2-$ , because each of Kumar et al., Salo 1 and Salo 2, teach their use in making oligonucleotide polymers on surfaces by linking the polymer building blocks to substrates, and cleavage of such disulfide-containing linkers to release the polymers, and because Lockhart et al. teach cleavage of linkers binding oligonucleotides libraries

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to substrates, and wherein the oligonucleotides are diverse members of large scale chemical arrays. One of ordinary skill in the art would have been motivated to use linkers having protecting groups that are photolabile, in order to create polymers using light-directed methods of polymer synthesis on solid substrates, as taught by Lockhart et al.

One of ordinary skill in the art would have had a reasonable expectation of success in making and using arrays of polymers on modified substrates comprising linker of the formula  $P^1-X^1-(W^1)_n-S-S-(W^2)_m-X^2-$ , because Kumar et al., Salo 1 and Salo 2, teach the use of such linkers and because the production of arrays of polymers on solid substrates using linkers, including linkers with photolabile protecting groups, was well known in the art at the time the invention was made.

### ***Conclusion***

9. Claims 23-29 and 31-34 are rejected.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark L. Shibuya whose telephone number is (571) 272-0806. The examiner can normally be reached on M-F, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571) 272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Mark L. Shibuya  
Examiner  
Art Unit 1639

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